

**REMARKS/ARGUMENTS**

Reconsideration of this application is requested. Claims 24-30, 36, 37 and 40 are in the case.

**I. THE 35 USC 112, FIRST PARAGRAPH, REJECTION**

Claims 24-30, 36, 37, 40 and 43 stand rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that the claims contain subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. The Examiner has further asserted that:

"A binding affinity of  $10^3 \text{ M}^{-1}$  would [sic] is not indicative of a high specificity for E2 or E3 in relation to any other protein in the cytosol of a cell because a binding affinity of  $10^3 \text{ M}^{-1}$  is deemed to be very low (see Harlow et al), this limitation is not sufficient to provide any kind of structural information regarding the ubiquitination recognition element."

This rejection is respectfully traversed.

The invention as claimed is directed to a method of reducing the level and/or activity of a target protein in an eukaryotic cell via the activation of ubiquitination of the target protein. The method comprises contacting the cell with a compound comprising (a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of the ubiquitination system, wherein the ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2

elements of a ubiquitination system of at least  $10^4 \text{ M}^{-1}$  and (b) a target protein binding element that is able to bind specifically to the target protein. The target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for the target protein greater than  $10^5 \text{ M}^{-1}$ . The ubiquitination recognition element is covalently linked to the target protein binding element.

The above methodology is fully described in the originally filed specification, beginning with the last complete paragraph on page 11 and extending through to page 13. Target protein binding peptide elements are described in detail beginning at page 22, and ubiquitination recognition elements are described beginning at page 29 of the specification. Specific examples of ubiquitination recognition elements are provided at pages 31-37, particularly page 34 first complete paragraph, and original claim 7.

One of ordinary skill in this art would understand the binding to the ubiquitination recognition element from basic education in biochemistry and biophysics, and would know how to obtain these binding species. In addition, the E2 and E3 elements are well known to persons of ordinary skill. The genome has been sequenced, and most of the E2 and E3 elements are available, either directly or via standard cloning methods known to persons of ordinary skill in the art. Moreover, all of the ubiquitination recognition elements can be joined to all target protein binding elements. While two such elements may be selected in ways that may involve challenging chemistry, it would not be impossible. One skilled in the art on reading the specification would understand that the specific methods used in the selection of these elements is important, and that the inventors were in possession of that subject matter when the case was filed.

On page 3 of the action, the Examiner has cited to examples of binding affinities of different types of molecules. The undersigned has been advised that many drugs are selected in drug screens at only  $10^3 \text{ M}^{-1}$ . Moreover, the comparison with antibodies is not appropriate given that they function in a very different way to the elements of the present invention. However, in order to expedite prosecution, and without conceding the merit of the Examiner's position, the claims have been amended without prejudice to specify that the ubiquitination recognition element has a binding affinity for the E3 and/or E2 elements of at least  $10^4 \text{ M}^{-1}$ . Basis appears at page 34 (end of first complete paragraph) and in original claim 7. No new matter is entered.

Based on the above, withdrawal of the 35 USC 112, first paragraph, rejection is believed to be in order. Such action is requested.

## **II. CLAIM INFORMALITY**

Claims 24 and 36 have been objected to as not providing proper antecedent basis for "the ubiquitination system". In the response filed on November 20, 2003, claims 24 and 36 were amended in the first paragraph to refer to "a ubiquitination system", thereby providing proper antecedent basis for subsequent references to the ubiquitination system. Withdrawal of the objection is respectfully requested.

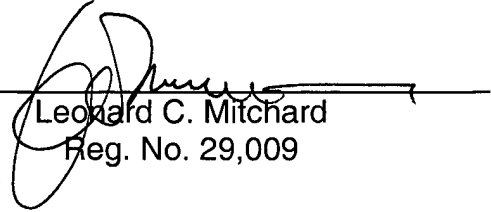
Allowance of the application is awaited.

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Respectfully submitted,

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By: \_\_\_\_\_



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